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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/519,731

07/05/2005

E Lucile White

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5125

23859

7590

09/26/2008

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EXAMINER

SRIVASTAVA, KAILASH C

ART UNIT

PAPER NUMBER

1657

MAIL DATE

DELIVERY MODE

09/26/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/519,731	Applicant(s) WHITE ET AL.	
	Examiner Dr. Kailash C. Srivastava	Art Unit 1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 03 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 May 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-42 is/are pending in the application.
- 4a) Of the above claim(s) 1-26,30,31 and 36-42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 27-29 and 32-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>07/05/2007</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The response and amendment filed 20 May 2008 to Office Action mailed 09 May 2008 is acknowledged and entered.

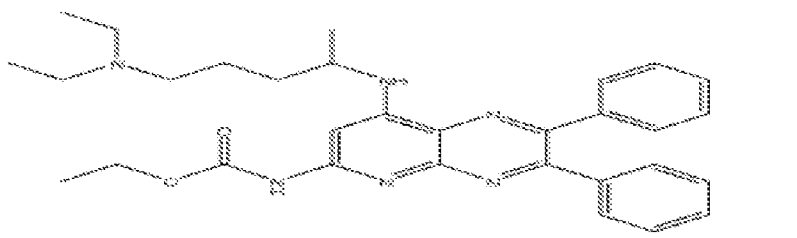
Claims Status

2. Claims 1-42 are currently pending.
3. Claim 27 has currently been amended.

Restriction/Election

4. The election without traverse of Group III invention, encompassing Claims 27-35 filed 05 February 2008 in response to Office Action mailed 24 October 2007 and reaffirmation of said election in response and amendment filed 20 May 2008 in response to the Office Action mailed 09 May 2008 is acknowledged and entered. Additionally, the species election of following species in response to Office Actions mailed 24 October 2007 and 09 May 2008 respectively is also acknowledged and entered.

- Only one chemical structure with substitutions to said chemical structure s listed in Claim 27 and under category I the elected species is: [8,(4-diethylamino-1-methyl-butylamino)-2,3-diphenyl-pyrido[2,3-b]pyrazine-6-yl]-carbonic acid ethyl ester (i.e., SRI-3072) with following structure:



- Only Gram positive bacteria reading on Claims 27-29 for species category J;
- Only Mycobacterium tuberculosis for the species category K; and
- Only Polymyxin B for the species category L;

according to the species election requirements of the Office Action mailed 24 October 2007.

Since both, the Group and the species elections are made without traverse; the restriction requirement is deemed proper and is made FINAL.

Accordingly, Claims 1-26, 30-31 and 36-42 and all other species in Claims 29, 33 and 35 but for those elected and recited *supra* are withdrawn from further consideration as being directed to a non-elected invention. See 37 C.F.R. §1.142(b) and M.P.E.P. §821.03.

5. Claims 27-29 and 32-35 are examined on merits.

Withdrawn Claims

6. Claims 1-26, 30-31 and 36-42 withdrawn from further consideration pursuant to 37 C.F.R. §1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 05/20/2008.

Priority

7. The claim for domestic priority under 35 U.S.C. §119(e) to U.S. Provisional application Serial Number 60/393,680 filed 02 July 2002 is acknowledged.

8. The claim for foreign priority under 35 U.S.C. §119(a-d) to PCT/US03/20984 filed 02 July 2003 is acknowledged.

Information Disclosure Statement

9. The Information Disclosure Statement (i.e., IDS) filed 05 July 2005 is acknowledged, has been made of record, considered and dully signed appropriate USPTO form is enclosed with the instant Office Action.

However, some of the incomplete reference citations (e.g., A73-A74), though considered, have not been initialed. Please re-submit a new USPTO Form 1449 or equivalent with indicated references with complete citation.

Objection to Specification

10. The specification is objected to because Line one of first page of specification, in its present form does not properly cite the application priority data. Please cite Claim of priority to the PCT application, as follows:

“This application claims foreign priority under 35 U.S.C. §119(a-d) to PCT/US03/20984 filed 02 July 2003.”

Claim Objection

11. Claim 27 as currently presented is objected to because the recitation, “[[d)]] or a salt thereof” at the end of Claim 27 is unclear. Is this line to be deleted or just the “d)”? Appropriate clarification/correction is requested.

Claim Rejections Under 35 U.S.C. §112

12. The following is a quotation of the second paragraph of 35 U.S.C. §112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

13. Claims 27-29 and 32-35 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 27 as currently presented is confusing and is therefore, unclear and vague. As a suggestion, please insert at Claim 27, line 2, the word--with--between the words, “bacterium” and “a” to clarify the claim 27.
- The current recitation of Markush groups at Claims 27 C), line three; 27 d) (I) line one; and 27d) (ii), line three renders Claim 27 unclear, vague and therefore indefinite. Please rewrite the Markush group in proper form, (i.e., “selected from the group consisting of”). Appropriate correction is required.
- The recitation, “gram” at line one of each of Claims 28-29 renders said Claims unclear, vague and indefinite. The art-acknowledged way of writing said word is “Gram” after the name of

the inventor who put forth the staining method to distinguish the two types of bacteria.

Appropriate correction is required.

- Claim 29 is rendered vague, unclear and indefinite because of the abbreviation (i.e., “M.”). Abbreviations in the first instance of claims should be expanded upon with the abbreviation indicated in parentheses. The abbreviations can be used thereafter. Examiner understands that the abbreviated terms are well-recognized in the art, still one of skill may not be able to clearly understand the claimed invention. Appropriate correction is required.
- The limitation, “enhancer” at Claim 33, line one lacks sufficient antecedent basis, because Claim 33 depends from claim 32, wherein the recited limitation is “permeability enhancer”. Appropriate correction/clarification is required.

All other claims depend directly, or indirectly from the rejected Claim 27 and are, therefore, also rejected under 35 U.S.C. § 112, second paragraph for the reasons set forth above.

Claim Rejections - 35 U.S.C. § 103

14. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

16. Claims 27-29 and 32-35 are rejected under 35 U.S.C. § 103 (a) as obvious over combined teachings from White et al., (2000. Slow Polymerization of *Mycobacterium tuberculosis* FTSE, Journal of Bacteriology, Volume 182, Pages 4028-4034, Cited in Applicants’ IDS filed 07/05/2007) in view of White et al (2002. 2-Alkoxy carbonylaminopyridines: inhibitors of *Mycobacterium tuberculosis* FTSE, Journal of Antimicrobial Chemotherapy, Volume 50, Pages 111–114, i.e., White et al’2) and further in view of Johnson et al (US Patent 6,319,958 B1).

Claims recite a method to inhibit polymerization of bacterial FtsZ by alkoxycarbonyl aminopyridine compound, wherein said FtsZ is from a Gram positive bacterium and further said Gram positive bacterium is *Mycobacterium tuberculosis*. Additionally, said compound is either linked to a “permeability enhancer” or said bacterium is contacted with a “permeability enhancer”, wherein said “permeability enhancer” is polymyxin B.

Regarding Claims 27-29 and 32-35, White et al. teach method to inhibit polymerization of *Mycobacterium tuberculosis* FtsZ by a tubulin polymerization inhibitor, (i.e., SRI 7614) having a structure similar to that of an 2-Alkoxycarbonylaminopyridine (Abstract, Lines 7-9). White et al, however, are silent about the polymerization of *Mycobacterium tuberculosis* FtsZ by [8, (4-diethylamino-1-methyl-butylamino)-2, 3-diphenyl-pyrido [2, 3-b] pyrazine-6-yl]-carbimic acid ethyl ester (i.e., SRI-3072), or putting the bacterial cell and the FtsZ inhibitor in contact with a permeability enhancer, e.g., polymyxin B.

White et al’2, however teach inhibition of polymerization of *Mycobacterium tuberculosis* FtsZ by 2-Alkoxycarbonylaminopyridine, wherein said compound is SRI 3072 and said SRI 3072 is also a tubulin polymerization inhibitor (Page 111, Column 1, Lines 30-31; Abstract, Lines 3-5, and Table 1). Johnson et al., teach method of sensitizing microbial cells to promote uptake of exogenous antimicrobial compounds by putting Gram positive bacterial cells in contact with permeability enhancers. They also teach contacting said bacterial cell with an antimicrobial compound and asesquiterpenoid (Abstract; Column 2, Lines 5-22; Column 4, Lines 19-21). Gram positive bacteria are preferred over Gram negative bacteria (Column 8, Lines 48-53). Note, despite being silent regarding the specific microorganism, Johnson et al., teach enhancing the uptake of an exogenous material in a Gram positive bacterial cell by putting said bacterial cell in contact with polymeric B.

One having ordinary skill in the art at the time of the claimed invention would have been motivated to modify/combine the teachings from White et al. according to the beneficial teachings from White et al’2’ and Johnson et al’s teachings to obtain a method to inhibit polymerization of bacterial FtsZ by alkoxycarbonylaminopyridine compound, wherein said FtsZ is from a Gram positive bacterium and further said Gram positive bacterium is *Mycobacterium tuberculosis*., wherefein said bacterium is in contact with a permeability enhancer, the permeability enhancer is polymyxin B; because both White et al., and White et al’2 teach inhibition of *Mycobacterium tuberculosis*’s FtsZ polymerization by a tubulin polymerization inhibitor which is alkoxycarbonylaminopyridine and White et al’2 specifically teach said alkoxycarbonylaminopyridine to be SRI3072. Johnson et al., teach a method of enhanced uptake of an

exogenous antimicrobial by a “permeability enhancer. The prior art references cited above do not enumerate each and every detail as claimed instantly with respect to different components//composition. However, adjustment of particular conventional working conditions (e.g., microbial organism, ceqialent compounds that inhibit certain physiological aspect in a Gram positive bacterium/ method steps etc.) is deemed merely a matter of judicious selection and routine optimization of a result-effective parameter that is well within the purview of the skilled artisan.

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify/combine the teachings from White et al., according to the beneficial teachings from White et al’2’ and Johnson et al’s teachings to obtain a method to inhibit polymerization of bacterial FtsZ by alkoxycarbonylaminopyridine compound, wherein said FtsZ is from a Gram positive bacterium and further said Gram positive bacterium is *Mycobacterium tuberculosis* wherein said bacterium is in contact with a permeability enhancer, the permeability enhancer is polymyxin B; because both White et al., and White et al’2 teach inhibition of *Mycobacterium tuberculosis*’s FtsZ polymerization by a tubulin polymerization inhibitor which is alkoxycarbonylaminopyridine and White et al’2 specifically teach said alkoxycarbonylaminopyridine to be SRI3072. Johnson et al., teach a method of enhanced uptake of an exogenous antimicrobial by a “permeability enhancer. This rejection is based on the well established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients, *In re Sussman*, 1943 C.D. 518. Instantly claimed invention is predicated on an unexpected result, which typically involves synergism, an unpredictable phenomenon, highly dependent upon specific proportions and/or amounts of particular ingredients. Any mixture of the components embraced by the claims which does not exhibit an unexpected result (e.g., synergism) is therefore *ipso facto* unpatentable.

Accordingly, the instant claims, in the range of proportions where no unexpected results are observed, would have been obvious to one of ordinary skill having the above-cited references before him.

From the teachings of the references cited *supra*, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

17. For reasons aforementioned, no Claims are allowed. However, Claims 32-33 may be free of the prior art. Claims 32-33 should be rewritten to overcome the rejection(s) under 35 U.S.C. §112, 2nd paragraphs, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims. Upon resolution of the above-stated issues under 35 U.S.C. §112, further searching and/or consideration may be required.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (571) 272-0923. The examiner can normally be reached on Monday to Thursday from 7:30 A.M. to 6:00 P.M. (Eastern Standard or Daylight Savings Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached on (571)-272-0925 Monday through Thursday. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding may be obtained from the Patent Application Information Retrieval (i.e., PAIR) system. Status information for the published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (i.e., EBC) at: (866)-217-9197 (toll-free). Alternatively, status inquiries should be directed to the receptionist whose telephone number is (703) 308-0196.

/Dr. Kailash C Srivastava/
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September 26, 2008
/David M. Naff/
Primary Examiner, Art Unit 1657